UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

000137

OCT 26

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

**MEMORANDUM**

SUBJECT: CIDEX OPA (0-phthaldehyde; EPA 129017) --- Acute Data on End-Use Product (EP), Submitted Under MRID # 412552-04 Thru - 08
EPA ID # 7078-RI.

Chemical (Caswell) 623C
RD Record No. 253, 113
HED Project No. 0-0338

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I (IRS)
Health Effects Division (H7509C)

10-03-90

TO: John H. Lee, PM 31
Antimicrobial Program Branch
Registration Division (H7505C)

THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I (IRS)
Health Effects Division (H7509C)

10/10/90

Registrant: Surgikos Inc., Arlington, TX

Request: Review and evaluate the following acute toxicity studies on CIDEX OPA Solution (an end-use product containing 0.56% o-phthaldehyde as a.i.), all performed for the registrant by TOXIKON CORPORATION, Woburn, MA:

(1) Acute Single Dose Oral Toxicity Study in Rats. (Unpublished Study No. 88G-0175, dated September 21, 1988; MRID No. 412552-04.)

(2) Single Dose Dermal Toxicity Study in Rabbits. (Unpublished Study No. 88G-0176; dated September 20, 1988; MRID No. 412552-05.)

(3) Primary Ocular Irritation Study in Rabbits. (Unpublished Study No. 88G-0177, dated September 15, 1988, MRID No. 412552-06.)

(4) Primary Dermal Irritation Study in Rabbits. (Unpublished Study No. 88G-0178, dated September 19, 1998; MRID No. 412552-07.)

(5) Epicutaneous skin sensitization test: Buehler topical closed patch technique (Unpublished study No. 88-0183, dated October 28, 1988; EPA MRID No. 412552-08.)

TB Conclusions: Following are TB's summary evaluations of these studies (detailed reviews are attached):

| Study Type (MRID) | Reported Results | TB Evaluation (Tox. Cat.) |
|---|---|---|
| (1) Acute oral-rat (412552-04) | $LD_{50}$ > 5000 mg/kg (males/females) | MINIMUM (IV) |
| (2) Acute dermal-rabbit (412552-05) | $LD_{50}$ > 2000 mg/kg (males/females) | MINIMUM (III) |
| (3) Primary eye irritation-rabbit (412552-06) | Moderate irritant (no corneal opacity; ocular irritation reversible within 7 days) | MINIMUM (III) |
| (4) Primary dermal irritation-rabbit (412552-07) | PSI = "0" (non-irritating; transient irritation disappearing by 72 hrs.) | MINIMUM (IV) |
| (5) Skin sentization-guinea pig (412552-08) | Not a sensitizer (no dermal reactions after induction or challenge) | SUPPLEMENTARY* (Concentration of agent not reported). |

*This study can be upgraded if concentration data are submitted.

ATTACHMENTS (DERs)

CONFIDENTIAL

EPA No.: 68D80056
DYNAMAC No.: 330-A
TASK No.: 3-30A
September 28, 1990

008137

# DATA EVALUATION RECORD

## CIDEX

## Acute Oral Toxicity Study in Rats

STUDY IDENTIFICATION: Lilja, H.S. Acute single oral toxicity aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0175 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 21, 1988.) MRID No. 412552-04.

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: William L. McLellan for

Date: 9/27/90

1. CHEMICAL: 1,4-Benzenedicarboxaldehyde/OPA, orthophthalaldehyde.

2. TEST MATERIAL: Aqueous o-phthalaldehyde solution, lot/batch No. 913-14-1, contained 0.56% active ingredient and was described as a light green liquid.

3. STUDY/ACTION TYPE: Acute oral toxicity study in rats.

4. STUDY IDENTIFICATION: Lilja, H.S. Acute single oral toxicity aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0175 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 21, 1988.) MRID No. 412552-04.

5. REVIEWED BY:

Patricia Turck, M.S.
Principal Reviewer
Dynamac Corporation

Signature: Patricia Turck
Date: September 28, 1990

Margaret E. Brower, Ph.D.
Independent Reviewer
Dynamac Corporation

Signature: Margaret Brower
Date: September 28, 1990

6. APPROVED BY:

Nicolas P. Hajjar, Ph.D.
Department Manager
Dynamac Corporation

Signature: William L. McLellan for
Date: Sept 28, 1990

Irving Mauer, Ph.D.
EPA Reviewer
Toxicology Branch I
(H-7509C)

Signature: Irving Mauer
Date: 10/02/90

Karl Baetcke, Ph.D.
EPA Branch Chief
Toxicology Branch I
(H-7509C)

Signature: Karl P. Baetcke
Date: 10/18/90

7. CONCLUSIONS:

CORE Classification: CORE Minimum. This study fulfills the minimum requirements set forth in EPA Guideline 81-1 for an acute oral toxicity study in rats.

$LD_{50}$: >5 g/kg for male and female rats.

Toxicity Category: IV.

8. SUMMARY: Five fasted Sprague-Dawley rats/sex (Charles River Breeding Laboratories, Inc., Wilmington, MA), weighing between 200 and 252 g, were administered single oral doses of aqueous o-phthalaldehyde solution at 5 g/kg in a volume of 5 mL/kg and observed for 14 days. Body weight was recorded on study days 0, 7, and 14, and animals were killed and subjected to a gross necropsy on study day 14.

No mortality occurred during the study. No clinical signs of toxicity or changes in body weight were observed. No abnormal findings were noted at necropsy. The study author classified the test material as nontoxic to rats.

9. REVIEWERS' COMMENTS AND QUALITY ASSURANCE MEASURES: The conduct and reporting of this study were adequate, except that a protocol was not provided. The $LD_{50}$ value was >5 g/kg, which is the limit required by EPA guidelines. The test material was classified in Toxicity Category IV. However, since the test material was only 0.56% pure, this may not have been an accurate indicator of acute oral toxicity of o-phthalaldehyde.

A signed quality assurance statement, dated September 21, 1988, was provided.

10. CBI APPENDIX: Not applicable.

EPA No.: 68D80056
DYNAMAC No.: 330-B
TASK No.: 3-30B
September 28, 1990

# DATA EVALUATION RECORD

## CIDEX

## Acute Dermal Toxicity Study in Rabbits

STUDY IDENTIFICATION: Lilja, H.S. Single dose dermal toxicity aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0176 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 20, 1988.) MRID No. 412552-05.

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: William L. McLellan for

Date: 9/27/90

1. CHEMICAL: 1,4-Benzenedicarboxaldehyde/OPA, orthophthalaldehyde.

2. TEST MATERIAL: Aqueous o-phthalaldehyde solution, lot/batch No. 913-14-1, contained 0.56% active ingredient and was described as a light green liquid.

3. STUDY/ACTION TYPE: Acute dermal toxicity study in rabbits.

4. STUDY IDENTIFICATION: Lilja, H.S. Single dose dermal toxicity aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0176 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 20, 1988.) MRID No. 412552-05.

5. REVIEWED BY:

Patricia Turck, M.S.
Principal Reviewer
Dynamac Corporation

Signature: Patricia Turck
Date: September 28, 1990

Margaret E. Brower, Ph.D.
Independent Reviewer
Dynamac Corporation

Signature: Margaret Brower
Date: September 28, 1990

6. APPROVED BY:

Nicolas P. Hajjar, Ph.D.
Department Manager
Dynamac Corporation

Signature: William L. McLellan for
Date: Sept. 28, 1990

Irving Mauer, Ph.D.
EPA Reviewer
Toxicology Branch I
(H-7509C)

Signature:
Date: 10/02/90

Karl Baetcke, Ph.D.
EPA Branch Chief
Toxicology Branch I
(H-7509C)

Signature:
Date: 10/18/90

7. CONCLUSIONS:

CORE Classification: CORE Minimum. This study fulfills the minimum requirements set forth in EPA Guideline 81-2 for dermal toxicity study in rabbits.

$LD_{50}$: >2 g/kg for male and female rabbits.

Toxicity Category: III.

8. SUMMARY: Single dermal applications of test material at 2 g/kg were administered to intact sites on the shaved backs (about 10% of total surface area) of five New Zealand white rabbits/sex (Pine Acres Rabbitry, Norton, MA), weighing between 2.13 and 2.67 kg. The test sites were semioccluded for 24 hours, after which the wrappings were removed, and the test sites were wiped and rinsed with water to remove remaining test material. Dermal irritation was scored after 24 hours of exposure, and overt signs of toxicity were recorded daily for 14 days. Body weight was recorded weekly.

No clinical signs of toxicity or reductions in body weight were observed during the study, and no rabbits died. No irritation was observed at 24 hours. The study author classified the test material as nontoxic.

9. REVIEWERS' COMMENTS AND QUALITY ASSURANCE MEASURES: The conduct and reporting of this study were adequate, except that a protocol was not provided. No mortalities were observed during the study, and therefore, the $LD_{50}$ value was >2 g/kg. This is the limit recommended by EPA guidelines. However, since the test material was only 0.56% pure, this study may not have been an accurate indicator of dermal toxicity of o-phthalaldehyde.

A signed quality assurance statement, dated September 20, 1988, was provided.

10. CBI APPENDIX: Not applicable.

NATIONAL [illegible]

EPA No.: 68D80056
DYNAMAC No.: 330-C
TASK No.: 3-30C
September 28, 1990

DATA EVALUATION RECORD

CIDEX

Primary Eye Irritation Study in Rabbits

STUDY IDENTIFICATION: Lilja, H.S. Primary ocular irritation study aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0177 conducted by Toxicon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 15, 1988.) MRID No. 412552-06.

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: William L. McLellan for

Date: Sept. 28, 1990



9

1. CHEMICAL: 1,4-Benzenedicarboxaldehyde/OPA; ortho-phthalaldehyde; cidex.

2. TEST MATERIAL: Aqueous o-phthalaldehyde solution, lot/batch No. 913-14-1, was 0.56% pure and described as a light green liquid.

3. STUDY/ACTION TYPE: Primary eye irritation study in rabbits.

4. STUDY IDENTIFICATION: Lilja, H.S. Primary ocular irritation study aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0177 conducted by Toxicon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 15, 1988.) MRID No. 412552-06.

5. REVIEWED BY:

Patricia Turck, M.S.
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Dynamac Corporation

Signature: Patricia Turck
Date: September 28, 1990

Margaret E. Brower, Ph.D.
Independent Reviewer
Dynamac Corporation

Signature: Margaret Brower
Date: September 28, 1990

6. APPROVED BY:

Nicolas P. Hajjar, Ph.D.
Department Manager
Dynamac Corporation

Signature: William L. McLellan for
Date: Sept 28, 1990

Irving Mauer, Ph.D.
EPA Reviewer
Toxicology Branch I
(H-7509C)

Signature: Irving Mauer
Date: 10/02/90

Karl Baetcke, Ph.D.
EPA Branch Chief
Toxicology Branch I
(H-7509C)

Signature: Karl D. Baetcke
Date: 10/18/90

7. CONCLUSIONS:

CORE Classification: CORE Minimum. This study fulfills the minimum requirements set forth under the EPA Guideline 81-4 for a primary eye irritation study in rabbits.

Primary Eye Irritation Rating: Moderate irritant.

Toxicity Category: III. No corneal opacity; ocular irritation reversible within 7 days.

8. SUMMARY: Three New Zealand white rabbits/sex (Pine Acres Rabbitry, Norton, MA), weighing 2.16-2.54 kg and free of ocular abnormalities, were administered 0.1 mL to the left eye; the right eye was untreated and served as a control. Eyes were scored for irritation at 1, 24, 48, and 72 hours and 4 days. Fluorescein staining was used at every examination except at 1-hour postdose. Animals were observed daily for overt signs of toxicity, and body weight was recorded on days 1 and 4 of the study.

Ocular irritation that included conjunctival redness and discharge was observed up to 72 hours postdosing. All dosed eyes were normal at 4 days postdosing. No corneal opacity, clinical signs of toxicity, or reductions in body weight were observed during the study. The study author classified the test material as a mild ocular irritant.

9. REVIEWERS' COMMENTS AND QUALITY ASSURANCE MEASURES: The conduct and reporting of this study were adequate, except that a protocol was not provided. The test material was classified in Toxicity Category III, moderately irritating, by the reviewers. However, since the test material contained only 0.56% active ingredient, this study may not have been an accurate indicator of the ocular toxicity of o-phthalaldehyde.

A signed quality assurance statement, dated September 15, 1988, was provided.

10. CBI APPENDIX: Not applicable.

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EPA No.: 68D80056
DYNAMAC No.: 330-D
TASK No.: 3-30D
September 28, 1990

# DATA EVALUATION RECORD

## CIDEX

## Primary Dermal Irritation Study in Rabbits

STUDY IDENTIFICATION: Lilja, H.S. Primary dermal irritation study aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0178 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 19, 1988.) MRID No. 412552-07.

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: William L. McLellan for

Date: Sept. 28, 1990

1. CHEMICAL: 1,4-Benzenedicarboxaldehyde/OPA; ortho-phthalaldehyde; cidex.

2. TEST MATERIAL: Aqueous o-phthalaldehyde solution, lot/batch No. 913-14-1, contained 0.56% active ingredient and was described as a light green liquid.

3. STUDY/ACTION TYPE: Primary dermal irritation study in rabbits.

4. STUDY IDENTIFICATION: Lilja, H.S. Primary dermal irritation study aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0178 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated September 19, 1988.) MRID No. 412552-07.

5. REVIEWED BY:

Patricia Turck, M.S.
Principal Reviewer
Dynamac Corporation

Signature: Patricia Turck
Date: September 25, 1990

Margaret E. Brower, Ph.D.
Independent Reviewer
Dynamac Corporation

Signature: Margaret Brower
Date: September 28, 1990

6. APPROVED BY:

Nicolas P. Hajjar, Ph.D.
Department Manager
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Signature: William L. McLellan for
Date: Sept. 28, 1990

Irving Mauer, Ph.D.
EPA Reviewer
Toxicology Branch I
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Signature:
Date: 10/02/90

Karl Baetcke, Ph.D.
EPA Branch Chief
Toxicology Branch I
(H-7509C)

Signature: Karl D. Baetcke
Date: 10/19/90

7. CONCLUSIONS:

CORE Classification: CORE Minimum. This study fulfills the minimum requirements set forth under EPA Guideline 81-5 for primary dermal toxicity study in rabbits.

Primary Dermal Irritation Index: 0. Nonirritating.

Toxicity Category: IV. Mild or slight irritation at 72 hours or no effects.

8. SUMMARY: Single dermal applications of 0.5 mL of the test material were administered to intact test sites on the shaved backs of three New Zealand white rabbits/sex (Pine Acres Rabbitry, Norton, MA) weighing 2.37-3.00 kg. A second test site was untreated and served as a control. The test sites (6 $cm^2$) were covered with a gauze patch, wrapped with bandaging, and exposed for 4 hours. After the exposure period, wrappings were removed and the test sites was carefully rinsed to remove remaining test material. Irritation was scored 30 to 60 minutes and 24, 48, and 72 hours after the exposure period. Body weight was recorded at study initiation and termination.

No dermal irritation was observed at any of the observation periods during the study. No reductions in body weight or clinical signs of toxicity were observed. The Primary Dermal Irritation Index was zero.

9. REVIEWERS' COMMENTS AND QUALITY ASSURANCE MEASURES: The conduct and reporting of this study were adequate, except that a protocol was not provided. However, since the test material was only 0.56% pure, this study may not have been an accurate indicator of dermal irritation of o-phthalaldehyde.

A signed quality assurance statement, dated September 19, 1988, was provided.

10. CBI APPENDIX: Not applicable.

008137

CONFIDENTIAL BUSINESS INFORMATION
EPA MAY CONTAIN
NATIONAL SECURITY INFORMATION (E.O. 12065)

EPA No.: 68D80056
DYNAMAC No.: 330-E
TASK No.: 3-30E
September 28, 1990

# DATA EVALUATION RECORD

## CIDEX

## Dermal Sensitization Study in Guinea Pigs

STUDY IDENTIFICATION: Lilja, H.S. Epicutaneous skin sensitization test (Buehler topical closed patch technique) aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0183 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated October 28, 1988.) MRID No. 412552-08.

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: William L McLelan for

Date: Sept. 28, 1990

1. CHEMICAL: 1,4-Benzenedicarboxaldehyde/OPA; o.tho-phthalaldehyde; cidex.

2. TEST MATERIAL: Aqueous o-phthalaldehyde solution, lot/batch No. 913-14-1, was 0.56% pure and described as a light green liquid.

3. STUDY/ACTION TYPE: Dermal sensitization study in guinea pigs.

4. STUDY IDENTIFICATION: Lilja, H.S. Epicutaneous skin sensitization test (Buehler topical closed patch technique) aqueous o-phthalaldehyde solution. (Unpublished study No. 88G-0183 conducted by Toxikon Corporation, Woburn, MA, and submitted by Surgikos, Inc., Arlington, TX; dated October 28, 1988.) MRID No. 412552-08.

5. REVIEWED BY:

Patricia Turck, M.S.
Principal Reviewer
Dynamac Corporation

Signature: Patricia Turck
Date: September 25, 1990

Margaret E. Brower, Ph.D.
Independent Reviewer
Dynamac Corporation

Signature: Margaret Brower
Date: September 28, 1990

6. APPROVED BY:

Nicolas P. Hajjar, Ph.D.
Department Manager
Dynamac Corporation

Signature: William L. McLellan for
Date: Sept 25, 1990

Irving Mauer, Ph.D.
EPA Reviewer
Toxicology Branch I
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Signature: Irving Mauer
Date: 10/02/90

Karl Baetcke, Ph.D.
EPA Branch Chief
Toxicology Branch I
(H-7509C)

Signature: Karl P. Baetcke
Date: 10/18/90

7. CONCLUSIONS:

CORE Classification: CORE Supplementary. This study meets the minimum requirements set forth under EPA Guideline 81-6 for a dermal sensitization study in guinea pigs. However, since the concentrations used in the induction and challenge phases were not reported, this study is considered only supplementary data. This study can be upgraded if concentration data are submitted.

8. SUMMARY: Groups of Duncan-Hartley guinea pigs (Harlan Sprague-Dawley, Indiana), weighing 213-276 g, were used. In a screening test designed to select dose levels for the challenge phase, the test material at concentrations of 25, 50, 75, and 100% was applied to four test sites on the backs of two male and two female guinea pigs. The exposure period was 24 hours, and irritation was scored 24 and 48 hours after the exposure period. No irritation was observed in any of these animals, and no toxicity or changes in body weights were noted.

For the induction phase, groups of 10 guinea pigs/sex received 0.5 mL of the test material (concentration not reported) three times/week for 3 consecutive weeks. The test sites were 2 cm x 3 cm and were located on the left shoulder of each guinea pig. The test sites were occluded for 6 hours, after which the patches were removed, and the test sites were washed off with warm water. In addition, a group of three guinea pigs/sex were administered 0.1 mL of 0.1% dinitro-chlorobenzene (DNCB) in acetone in a similar manner and served as positive controls. On week 5, the challenge dose (concentration not reported) was applied to a virgin site (2 cm x 2 cm), using either the test material (test group) or DNCB (positive control group), and the test sites were occluded for 24 hours. After the exposure period, the entire back of each guinea pig was shaved, and at 2, 48, and 72 hours after shaving, the test sites were scored for skin reactions. Body weights were recorded at initiation and termination of the study. Animals were observed daily for overt signs of toxicity.

No dermal reactions were observed after application of the challenge dose of the test material. DNCB-treated animals exhibited a dermal response at 2 hours, which worsened at 48 and 72 hours postchallenge. The study author classified the test material as a nonsensitizer.

9. REVIEWERS' COMMENTS AND QUALITY ASSURANCE MEASURES: The conduct and reporting of this study were adequate, except that a protocol was not provided. Furthermore, the study author did not report the concentration of test material used for either the induction or challenge phases. Therefore, the reviewers

could not determine if the test animals were sufficiently challenged. This study is considered supplementary data only.

A signed quality assurance statement, dated October 28, 1988, was provided.

10. CBI APPENDIX: Appendix, Test Procedures, CBI pp. 7-10.

# APPENDIX

## Test Procedures

(CBI pp. 7-10)

*Pages 20-23 Access to FIFRA health and safety data is restricted under FIFRA section 10(g)*

# END